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# TALL LARKSPUR INGESTION: CAN CATTLE REGULATE INTAKE BELOW TOXIC LEVELS?[1]

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**Abstract**—Tall larkspur (*Delphinium barbeyi*) is a toxic forb often consumed by cattle on mountain rangelands, with annual fatalities averaging about 5%. This study examined the relationship between food ingestion and toxicity in cattle. Two grazing studies suggested that larkspur consumption above 25–30% of cattle diets for one or two days led to reduced larkspur consumption on subsequent days. We subsequently hypothesized that cattle can generally limit intake of larkspur to sublethal levels. This hypothesis was tested by feeding a 27% larkspur pellet in experiment 1. Cattle given a 27% larkspur pellet ad libitum showed distinct cyclic patterns of intake, where increased larkspur consumption on one or two days was followed by reduced ($P < 0.025$) consumption on the following day. The amount of larkspur (mean 2007 g/day; 17.8 mg toxic alkaloid/kg body wt) consumed was just below a level that would produce overt signs of toxicity. Experiment 2 was conducted to examine cattle response to a toxin dose that varied with food intake. Lithium chloride (LiCl) paired with corn ingestion was used as a model toxin, and we hypothesized that if increased (decreased) consumption was followed by a stronger (weaker) dose of LiCl, cattle would show a transient reduction (increase) in corn intake. There was no difference ($P > 0.05$) between controls and treatment animals at the 20 or 40 mg LiCl/kg dose in the percentage of

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[1]All experimental procedures with animals followed guidelines approved by the Utah State University Animal Care and Use Committee and were conducted under veterinary supervision.



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corn consumed, but the 80 mg LiCl/kg dose induced a cyclic response (mean 46%) compared to intake by controls (mean 96%) ($P < 0.001$). At the 80 mg/kg dose, LiCl induced an aversion to corn; when corn intake decreased on subsequent days and LiCl dose also decreased, cattle responded by increasing corn intake and apparently extinguishing the transient food aversion. Experiment 3 was similar to the LiCl trial, except that tall larkspur was the toxin. Cattle responded to oral gavage of ground larkspur with distinct cycles; days of higher corn consumption were followed by one to three days of reduced consumption. Corn intake for controls was higher ($P < 0.01$) than for larkspur-treated animals (means 84 and 52%, respectively; day × treatment interaction $P < 0.01$). The threshold for toxic effects on corn intake was 14 mg toxic alkaloid/kg body weight. In conclusion, cattle apparently limit ingestion of some toxins so that periods of high consumption are followed by periods of reduced consumption to allow for detoxification. Cyclic consumption generally enables cattle to regulate tall larkspur consumption below a toxic threshold and allows cattle the opportunity to safely use an otherwise nutritious, but toxic, plant.

**Key Words**—Larkspur, alkaloids, intake regulation, toxicity, cattle.

## INTRODUCTION

Generalist herbivores may regulate ingestion of food and minimize aversive feedback from toxins. For instance, aversive postingestive feedback caused cattle to reduce intake of tall larkspur (*Delphinium barbeyi*), a forb that contains toxic alkaloids (Pfister et al., 1990). The extent of larkspur ingestion appeared to be limited by the concentration of toxic alkaloids. Olsen and Ralphs (1986) were also able to cause strong food aversions to a familiar food in cattle by using large doses of alkaloid extracts from tall larkspur. Nausea may be one basis for aversive postingestive feedback in livestock (Provenza et al., 1992). In the case of larkspur, nausea may be the result of larkspur alkaloids inhibiting the function of cholinergic parasympathetic nerves of the gastrointestinal tract, similar to nicotine-induced nausea (Taylor, 1990).

Larkspur contains numerous diterpenoid alkaloids, but the principal toxic alkaloids are methyllycaconitine (MLA) and 14-deacetylnudicauline (DAN) (Manners et al., 1992). These two alkaloids are similar in toxicity ($LD_{50} \approx 4.5$ mg/kg in mice; Manners et al., 1995), and account for most of the toxicity of tall larkspurs (Panter and Manners, unpublished data). The larkspur alkaloids block acetylcholine (ACh) receptors in the central and peripheral nervous system (Benn and Jacyno, 1983; Dobelis et al., 1993), eventually leading to muscular weakness, paralysis, and death from respiratory failure. Of course, the toxin dosage while foraging depends on the amount and toxicity of the plant ingested.

In this paper, we first provide a retrospective analysis of individual animal records for the pattern of larkspur ingestion by cattle foraging on rangelands. On the basis of that analysis, we hypothesized that cattle can limit intake of some toxic foods to sublethal levels. We tested this hypothesis experimentally in the following three experiments.

*Experiment 1: Cyclic Consumption of Larkspur Pellets by Cattle.* The objective of this experiment was to determine if cattle consumption of larkspur pellets followed a cyclic pattern, indicating subclinical intoxication and detoxification. We hypothesized that since larkspur is very nutritious (Pfister et al., 1989), animals may immediately experience positive postingestive consequences, followed by delayed adverse gastrointestinal illness due to alkaloids or other secondary compounds (Provenza et al., 1992). This delayed illness may reduce food consumption until toxicity passes, then animals may show an increasing propensity to consume larkspur, presumably due to positive nutritional feedback.

*Experiment 2: Food Ingestion as Affected by LiCl.* Conditioned food aversion studies have shown that cattle can be trained to avoid tall larkspur if illness (i.e., nausea induced by LiCl) is paired with larkspur ingestion (Lane et al., 1990; Ralphs, 1992). If cattle sample the plant, however, the aversion is eventually extinguished (Ralphs and Olsen, 1990; Lane et al., 1990). Sheep also continue to sample harmful foods after experiencing illness from ingesting the food (Burritt and Provenza, 1989). Launchbaugh et al. (1993) found that lambs could detect levels of LiCl mixed with barley and would adjust feed intake to a level slightly below the amount necessary to induce a food aversion. This study was done to examine cattle response to a toxin dose that varied with food intake. We used LiCl because this compound produces rapid emesis without other undesirable side effects. The objective of this experiment was to determine if cattle would adjust intake when food consumption was paired with gastrointestinal distress produced by LiCl, and no change in flavor cues were present to predict toxicity. We hypothesized that if increased consumption was followed by a stronger dose of LiCl, animals would show a transient reduction in intake of the food.

*Experiment 3: Food Ingestion as Affected by Tall Larkspur.* This experiment was conducted in a similar manner to experiment 2, except that tall larkspur replaced LiCl as the toxic agent. The objective of this experiment was to determine if cattle would adjust intake when novel food consumption was paired with subclinical toxicosis produced by tall larkspur. We hypothesized that if increased consumption of the novel corn was followed by a higher dose of larkspur alkaloids, animals would show a transient reduction in corn intake.

## METHODS AND MATERIALS

*Retrospective Study of Larkspur Ingestion by Individual Grazing Animals.* Grazing studies were conducted during 1986 and 1987 with Hereford cows to determine when cattle consumed tall larkspur in relation to plant alkaloid levels

(Pfister et al., 1988a,b). These studies provided mean daily larkspur consumption by groups of animals. We retrospectively examined records of individual animals from those studies to determine if any larkspur consumption patterns were apparent. Detailed methods for the field grazing trials are given in Pfister et al. (1988a,b). Both grazing trials were conducted on the Manti-LaSal National Forest at about 3000 m elevation. Plant communities were dominated by patches of tall larkspur. During both years, all animals were focally sampled in a predetermined random order during all active grazing periods. The same animals were used each year. Bite counts were used to determine diet composition (i.e., percent of bites); diets were categorized as grasses, forbs, shrubs, and larkspur. Tall larkspur was in the flower and pod stages of growth during these two studies.

*Experiment 1: Cyclic Consumption of Larkspur Pellets by Cattle.* Tall larkspur was collected from high elevation ( >3000 m) rangeland in central Utah during the summer of 1989. Plants were air-dried, ground through a 2-mm screen, and mixed with alfalfa hay to form a 27% larkspur pellet. We chose to make 27% pellets because cattle often consumed 25–30% of their diets as larkspur (Pfister et al., 1988a,b). Toxic alkaloid content of the larkspur pellet was determined using HPLC (Manners and Pfister, 1993).

Ten 32-month old Hereford × Angus heifers weighing 412 ± 56 kg were used in the study during the fall of 1989. Feed intake was monitored using locking head stanchions with individual feeders. Animals were habituated to being locked into the stanchions each morning at 0800 hr, and were allowed to eat until 1100 hr. Alfalfa pellets were fed ad libitum for 10 days to all animals to establish a baseline; consumption was stable on days 8–10. Feed intake was measured as the difference between feed offered and that remaining after 3 hr.

Cattle were randomly divided into two groups ($N$ = 5); the control group was fed only alfalfa pellets ad libitum for nine days. Subclinical larkspur intoxication produces no measurable biochemical lesions or quantifiable diagnostic signs, thus reductions in feed intake were used as an index of intoxication for the larkspur group. Consumption was compared to the last three days of baseline for alfalfa, when intakes had stabilized, by calculating daily consumption as a percentage of baseline (100%). Percentage values were analyzed using ANOVA with repeated measures over days.

*Experiment 2: Food Ingestion as Affected by LiCl.* Twelve 2-year-old Charolais × Angus × Hereford cows (431 × 35 kg) that were ruminally cannulated were given 35 days to become familiar with alfalfa pellets and were allowed ad libitum access to alfalfa pellets from 1300 to 1500 hr each day. Whole shelled corn, a highly palatable but novel food, was used as the target food.

Cattle were randomly divided into controls and a treatment group ($N$ = 6) and remained in the same group throughout the study. We began with a low dose of LiCl (20 mg/kg body weight) for eight days, then increased the dose (40 mg/kg body weight) for 11 days, and ended with a high dose (80 mg/kg) for eight days. A dose of 100 mg/kg body weight induces mild aversion to a novel food (Ralphs and Cheney 1993). We extended the 40 mg LiCl dose for an extra three days because food intake of two animals began to fluctuate near the end of the eight-day period.

Corn (1000 g) was offered for 10 min at 0800 hr, and LiCl was administered intraruminally in 100 ml of water in proportion to the amount of corn consumed and the body mass of the animal. For example, during the 20 mg/kg body weight period, if a 400-kg animal consumed 500 g of corn (50% of corn offered), it was immediately dosed intraruminally with 4 g of LiCl (50% dose). Provenza et al. (1993) found that LiCl levels peaked rapidly (i.e., within 15 min) when given intraruminally to sheep. Cattle could easily consume 1000 g of corn in a 10-min period. Each period was analyzed separately using a split-plot ANOVA model, with repeated measures over days.

*Experiment 3: Food Ingestion as Affected by Tall Larkspur.* Ten 3- to 4-year-old Hereford × Angus cows (598 × 42 kg) were randomly assigned to two treatment groups ($N = 5$). These cows had all grazed on summer range where they had ingested some tall larkspur.

After an initial seven-day period with ad libitum access to alfalfa pellets, a familiar food, ad libitum pellet intake was measured for each animal for 10 days, and mean intake over the last five days constituted the baseline value. Thereafter, alfalfa pellets were offered at 90% of baseline to each animal individually from 1300 to 1500 hr each day.

Tall larkspur (*D. barbeyi*) was collected from the Wasatch Plateau at 3200 m elevation in late July, 1994, air-dried at 20°C, ground through a 2-mm screen, and stored at 16°C in sealed plastic bags. Larkspur was analyzed by an HPLC method to determine toxic alkaloid concentration (Manners and Pfister, 1993).

Whole, shelled corn (1000 g) was offered to each animal individually in a food box for 5 min/day at 0700 hr. Cattle had to eat avidly to consume all the corn within 5 min. Immediately thereafter, cattle were dosed with either ground larkspur or ground alfalfa via oral gavage in direct proportion to the amount of corn consumed. The amount of larkspur that was dosed varied as a function of the amount of corn eaten. A 100% larkspur dose was equivalent to 16 mg toxic alkaloid/kg body weight; alfalfa was dosed to controls at the equivalent amount of 2.22 g/kg body weight. This dose of tall larkspur was estimated to be just below an amount ($>22$ mg/kg) that would cause muscular weakness and possible temporary collapse (Pfister et al., 1994b). The onset of overt toxicosis from tall larkspur is generally delayed by 7–10 hr from time of ingestion (Pfister et al., 1994c), so cattle would presumably have experienced illness from tall larkspur during midafternoon. Livestock can acquire taste aversions if the delay between food ingestion and postingestive consequences does not exceed 12 hr (Burritt and Provenza, 1989).

The experiment was analyzed as a repeated-measures ANOVA with treatment, animals nested with treatment, with a day effect, and the day × treatment interaction. When a significant $F$ test was found ($P < 0.05$), the PDIFF procedure of SAS (1987) was used to separate means.

## RESULTS

*Retrospective Study of Larkspur Ingestion by Individual Grazing Animals.* Larkspur consumption by individual animals in the 1986 and 1987 studies varied in a cyclic pattern, generally over a two- to four-day period (Figure 1). In both studies, there was a significant day effect ($P < 0.01$). During the 1986 study, cattle ate substantial amounts of larkspur early in the grazing period, whereas larkspur consumption was initially low during 1987 before increasing over time. Overall, the pattern of consumption suggests that when larkspur was ingested at levels above 25–30% of the diet during a specific day, cattle decreased consumption over the next day or two.

*Experiment 1: Cyclic Consumption of Larkspur Pellets by Cattle.* Intake of alfalfa pellets was low during the first few days of the trial, until daily consumption leveled to about 10 kg/head by day 8–10 (Figure 2). Toxic alkaloid concentration of the 27% larkspur pellet was 1.06 mg toxic alkaloid/g (3.92 mg/g in plant). Previous toxicity tests have shown that no overt signs of intoxication (i.e., muscular tremors, periodic collapse) are apparent unless cattle are given a single pulse dose equivalent to about 2300 g larkspur ( >22 mg toxic alkaloid/kg body weight) (Pfister et al., 1994b). In this trial, no overt signs of intoxification were noted, presumably because cattle ate the pellets over several hours. Mean larkspur intake was 2007 g/day.

Cattle given only the 27% larkspur pellet showed distinct cycles of increasing consumption, a period of rejection, and increased intake again (Figure 2; day × treatment interaction, $P < 0.025$). Intake by controls ranged from 93 to 115% of baseline, whereas intake by larkspur animals ranged from 53 to 97% of baseline. Controls averaged 105% of baseline; the larkspur group averaged 79% ($P < 0.008$).

*Experiment 2: Food Ingestion as Affected by LiCl.* All animals ate 100% of the basal ration except for one treatment animal that refused about 1.5 kg of alfalfa pellets on days 6 and 7 during the 40-mg dose and on day 4 during the 80-mg dose. No differences in corn consumption ($P > 0.1$) between treatment and controls were found at the 20 or 40 mg/kg dose of LiCl (Figure 3). There was a day effect and day × treatment interaction for corn intake ($P < 0.01$)

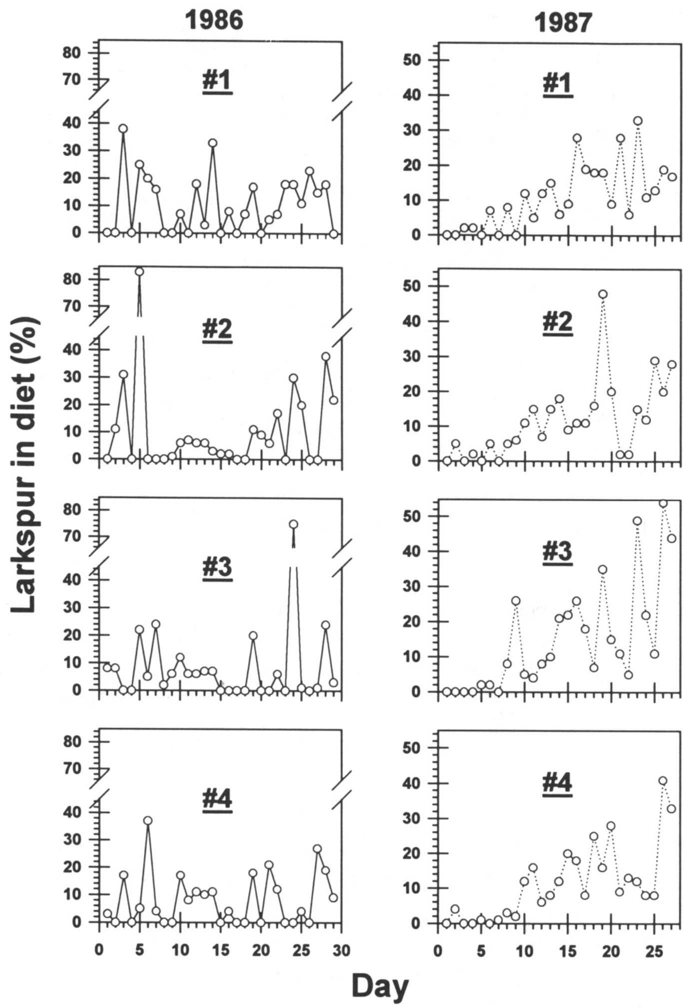


FIG. 1. Consumption of tall larkspur (% of diets) by individual heifers, numbered 1 to 4, grazing in Utah during summer, 1986 and 1987. The same animals were used both years. Both trials began when larkspur was in the flower stage and ended when larkspur was in the pod stage.

for the 20 mg/kg dose, due mainly to initial variability in acceptance of a novel food. Corn intake for the control and treatment groups differed at the 80 mg/kg dose ($P < 0.001$, Figure 3). There was a day effect ($P < 0.001$) and a day × treatment interaction at this dose ($P < 0.03$). At the 80-mg level, the controls averaged over 96% consumption of the corn, while the treatment group averaged

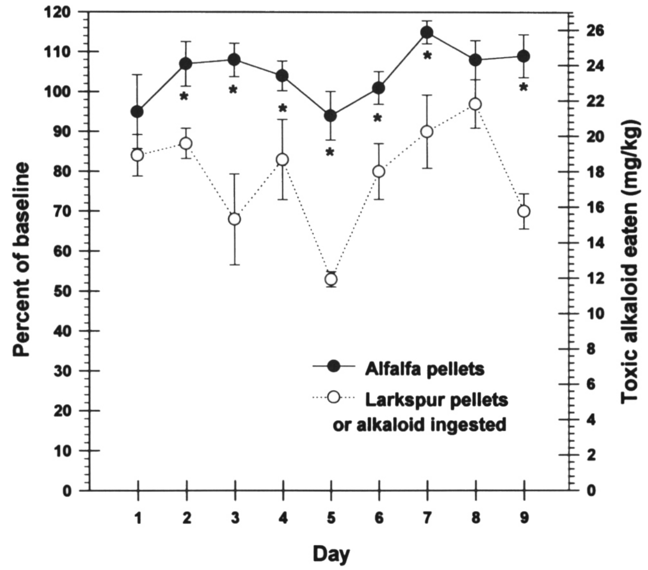


FIG. 2. Experiment 1: pellet consumption (% of baseline on left $y$ axis) by cattle receiving either larkspur pellets (treatment group), or alfalfa pellets (controls) during a nine-day pen trial. The right-hand $y$ axis is mean daily amount of toxic alkaloid ingested per kilogram of body weight and applies only to animals receiving larkspur pellets. Bars are $\pm$SE for pellet consumption. An asterisk indicates a difference ($P < 0.05$) between controls and treatment groups for pellet consumption.

only 46% corn consumption. The LiCl group decreased corn intake to below 20% by day 3, then intake increased to 40–50% of the offered corn from days 5 to 8.

Cattle on the 80 mg/kg dose received an average daily dose of 37 mg LiCl/kg. Cattle generally did not refuse any alfalfa pellets in the afternoon after being dosed with the 80-mg dose of LiCl in the morning, indicating that only corn intake was affected by LiCl. Most animals who received the 80-mg dose decreased corn intake on days 2 and 3, then increased corn intake in a fluctuating manner. An actual dose of about 60–70 mg LiCl/kg body weight on one or two days would result in decreased corn consumption on subsequent days. Because all animals on the 80-mg dose were not in sync with respect to daily fluctuations after day 3, two patterns representative of individual animal variability are shown in Figure 4. One animal (Figure 4A) was apparently more susceptible in LiCl than the other animals, and corn consumption by that animal fluctuated greatly at the 40-mg dose. The 40-mg dose apparently induced a transient aversion, whereas the 80-mg dose also induced an aversion interspersed with several days

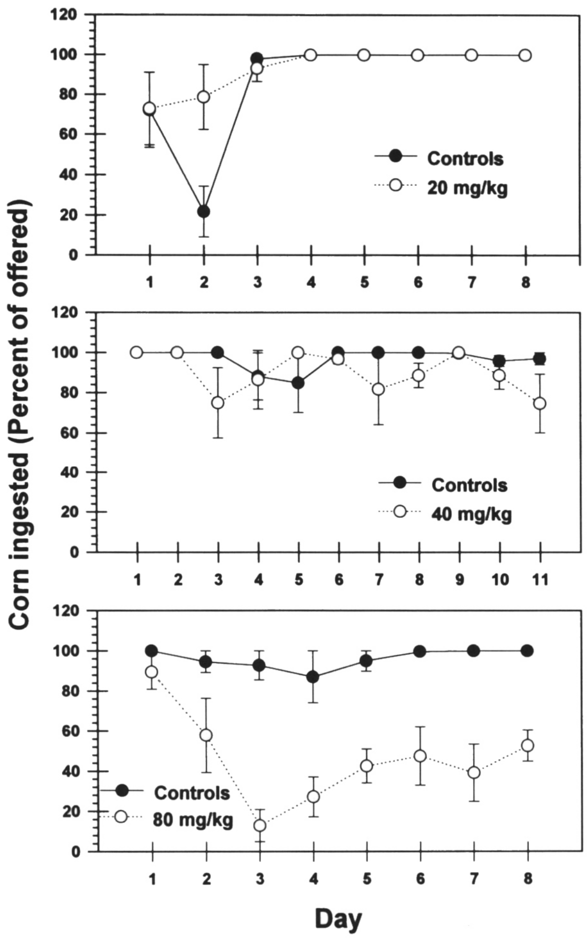


FIG. 3. Experiment 2: consumption of corn (% of 1000 g offered) during a 10-min trial when corn consumption was followed by an intraruminal dose of 20, 40, or 80 mg LiCl/kg body weight or no treatment was given (controls). At each dose level, LiCl was dosed in proportion to the amount of corn consumed during each period. At the 80-mg dose, the treatment and control groups differed ($P < 0.05$) each day after day 1. There was a treatment × day interaction ($P < 0.05$) at the 20- and 80-mg doses and no interaction at the 40 mg dose. Bars are ±SE for corn intake.

of acceptance of corn (Figure 4B). Conversely, the other animals were generally not affected by the 40-mg dose (Figure 4C), but showed distinct cyclic patterns when receiving the 80-mg dose (Figure 4D).

*Experiment 3: Food Ingestion as Affected by Tall Larkspur.* There was a

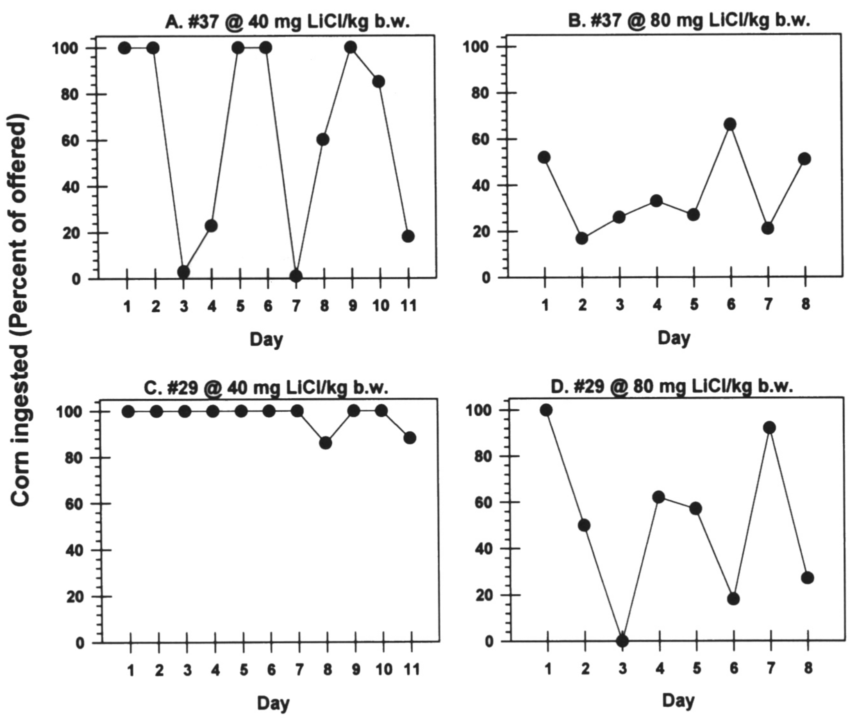


FIG. 4. Experiment 2: daily corn consumption (% of 1000 g offered) by animals #37 (A and B) and #29 (C and D) during a 10-min trial for eight days using either 40 or 80 mg LiCl/kg body weight. During each period, LiCl was dosed in proportion to the amount of corn consumed.

treatment effect ($P < 0.01$) and a day × treatment interaction ($P < 0.01$) for corn consumption (Figure 5). Overall, corn intake was lower ($P < 0.01$) for the larkspur group compared to controls (52 vs. 84%, respectively). Daily corn intakes for each individual animal are shown in Figure 6. Corn intakes were generally low initially because of its novelty, but some animals were not initially neophobic to corn. Larkspur animals showed various cyclic patterns of corn intake; in general one to three days of higher corn consumption (and higher larkspur doses) were followed by one to three days of reduced corn consumption. For most treatment animals the threshold for larkspur effects on food intake was about 14 mg/kg body weight. One animal (#6) did not respond to the 16 mg/kg dose of larkspur, so her dose was increased to 20 mg/kg on day 8, after which she showed a cyclic pattern of intake. The tall larkspur in this collection had a toxic alkaloid concentration of 7.2 mg/g. No overt signs of toxicosis were noted during the experiment. One control animal (#49) was injured by another cow on day 13 and was removed from the study.

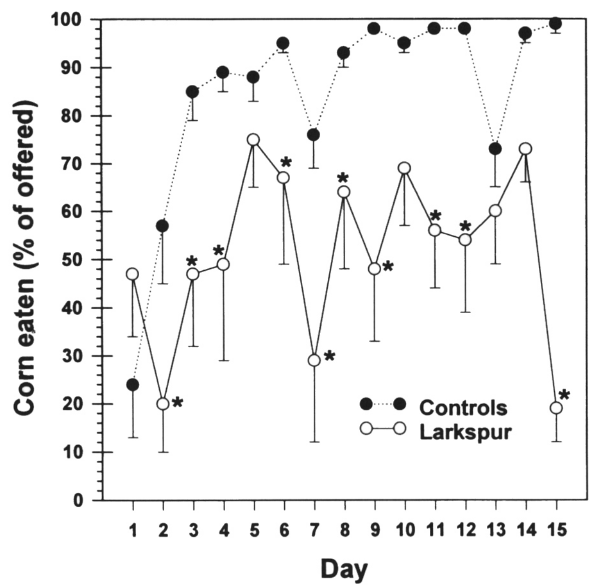


FIG. 5. Experiment 3: mean consumption of corn (% of 1000 g offered) during a 5-min trial when corn consumption was followed by an oral dose of tall larkspur (larkspur) or alfalfa (controls). Larkspur and alfalfa were dosed in proportion to the amount of corn consumed. An asterisk indicates that the larkspur group differs ($P < 0.05$) from controls. There was a treatment × day interaction ($P < 0.01$). Bars are −SE.

There was no difference in alfalfa pellet consumption ($P > 0.1$) between the two groups, nor was there a day × treatment interaction ($P > 0.4$). Mean alfalfa pellet intake was 95% of that offered, which again shows that the aversion was specific to the corn.

## DISCUSSION

*Retrospective Study of Larkspur Ingestion by Individual Grazing Animals.* Individual animal consumption of toxic plants is often overlooked and is of paramount importance in understanding how animals react to toxins (Provenza et al., 1992). Diets of grazing ruminants vary within and between days; this grazing strategy is thought to provide sufficient nutrients (Kyriazakis and Oldham, 1993; Provenza, 1995), avoid food-specific satiety or toxicity (Provenza, 1995), and alleviate dietary monotony (Newman et al., 1992; Early and Provenza, unpublished data, 1996). A major mechanism for dietary variety may be acquired aversions for both nutritious and toxic foods, which diminish preferences for selected foods (Provenza, 1996). The cyclic pattern noted in Figure

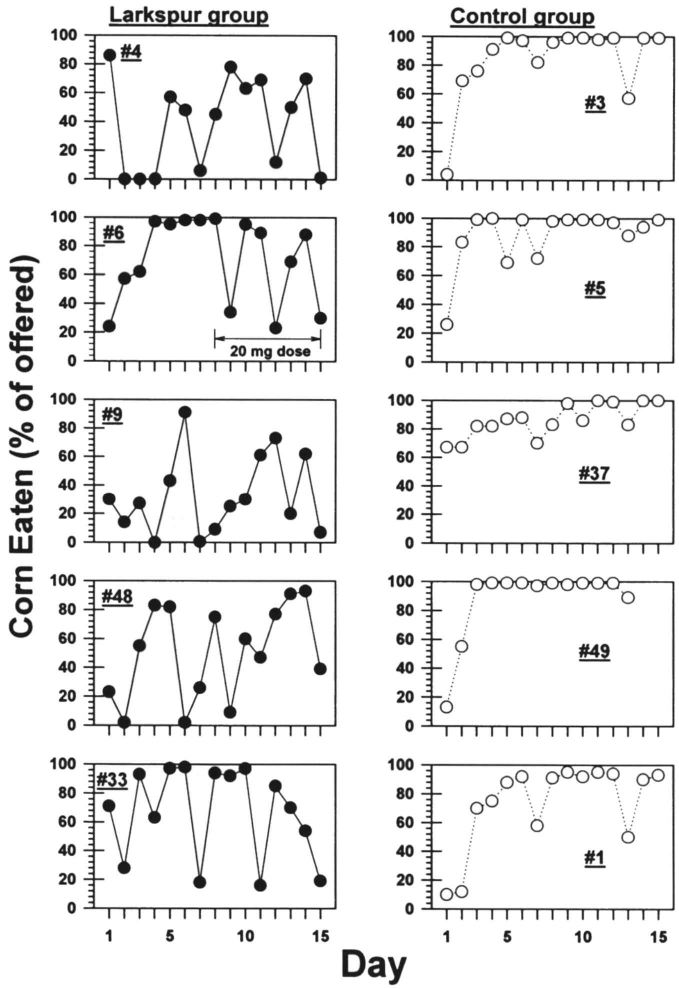


FIG. 6. Experiment 3: daily corn consumption (% of 1000 g offered) by individual animals in the larkspur-treated group and controls. The tall larkspur dose was 16 mg toxic alkaloids/kg body weight for all animals except where noted for animal #6; the corresponding alfalfa dose for controls was 2.2 g/kg body weight. Control animal #49 was injured by another animal and removed from the study after day 13.

1 appears to be a specific response to tall larkspur. The data suggest that cattle ingest larkspur up to some critical threshold, then reduce larkspur intake, which presumably allows a detoxification period. We have examined daily grazing records of cattle consumption of other major palatable forbs (e.g., tall bluebell, *Mertensia arizonica*; cow parsnip, *Heracleum lanatum*). Variability is evident

as one would expect, but cyclic changes are not apparent as with tall larkspur (Pfister, unpublished data). These observations provided a rationale for three pen studies to examine cattle consumption patterns of either tall larkspur or food ingestion paired with toxic larkspur or LiCl.

*Experiment 1: Cyclic Consumption of Larkspur Pellets by Cattle.* Cattle in the larkspur group ingested pellets in amounts (mean 7628 mg toxic alkaloid; 17.8 mg toxic alkaloid/kg body weight) near the threshold for overt toxic symptoms (9400 mg toxic alkaloid, >22 mg/kg) (Pfister et al., 1994a; Pfister and Cheney, 1997). The results suggest that under these conditions cattle can regulate consumption of larkspur and therefore generally avoid overingestion and overt intoxication. One to several days of high consumption were followed by a day of reduced consumption. These periods of reduced consumption apparently allow animals to recover from subclinical larkspur toxicity. Because MLA and DAN reversibly bind to ACh receptors (Dobelis et al., 1993), the degree of intoxication will depend on receptor site saturation, ACh and toxin concentration and subsequent competition in the synaptic cleft, and alkaloid binding affinity to ACh receptors. The rate of detoxification will depend primarily on toxin concentration, metabolism, and excretion at the active site (Lefkowitz et al., 1990). We have previously found that cattle recover within 24–48 hr after being dosed with sufficient larkspur alkaloids to produce muscular tremors and recumbency (Pfister et al., 1994b).

*Experiment 2: Food Ingestion as Affected by LiCl.* Within each experimental period (i.e., 20-, 40-, or 80-mg dose), the amount of LiCl actually dosed to each animal depended upon how much corn was consumed. Thus, on days when corn consumption was very low or very high, the amount of LiCl was varied accordingly. This scenario resembles grazing conditions, where the amount of toxic alkaloids ingested depends primarily on the amount of larkspur consumed, since alkaloid levels change only gradually over the growing season (Pfister et al., 1988b, 1994a; Pfister and Manners, 1991).

The results suggest that cattle can generally regulate intake of LiCl below an individual threshold of about 60–80 mg/kg. Four of six animals required ≥70 mg/kg for two consecutive days before intakes decreased, whereas a fifth animal reduced intake after one 67 mg/kg dose, and the sixth animal reduced intake after an initial dose of 41 mg/kg. Once the individual threshold was reached, animals reduced corn intake for one to three days, but began consuming some corn again when LiCl dosage decreased. The aversion to corn paired with LiCl was fragile, probably because 80 mg (the highest dose used) is not a particularly strong dose (Ralphs and Cheney, 1993) and perhaps due to positive postingestive feedback from corn. Corn is high in digestible energy and provides rapid postingestive reinforcement (Villalba and Provenza, 1997).

*Experiment 3: Food Ingestion as Affected by Tall Larkspur.* Tall larkspur doses paired with corn consumption resulted in transient aversions at higher amounts. Cattle apparently sense tall larkspur toxicosis and make an association between the larkspur dose and the corn flavor. This aversion is fragile, however, as subsequent sampling of corn generally leads to rapid extinction and heightened corn intake during later tests. We suspect that the aversion was not strong or permanent because the nausea was relatively mild (e.g., animals did not reduce basal feed intake), and because the positive feedback from corn encouraged renewed consumption. These results with corn and larkspur are similar to the patterns noted in grazing cattle (Figure 1). Cattle apparently have the ability to moderate tall larkspur intake based on gastrointestinal feedback from larkspur, even though ingestion and toxicosis may not be closely linked in time. This experiment also indicates that overall food intake is not adversely affected by subclinical larkspur toxicosis. We have noted in other studies (Pfister et al., 1994c; Pfister and Cheney, 1997) that food intake (i.e., long-stem hay) is reduced for two or three days after cattle show overt signs of intoxication, including muscular tremors and periodic collapse.

*General Discussion.* Cattle regulated consumption of larkspur following intoxication. Grazing animals showed marked fluctuations in amounts of larkspur consumed; one or two days of high consumption were generally followed by a day or two of reduced consumption. During experiment 1, cattle followed days of high consumption of larkspur pellets with a day of reduced consumption; average daily consumption (17.8 mg toxic alkaloid/kg) was just below a toxic threshold, above which cattle show overt signs of intoxication. In experiments 2 and 3, cattle displayed similar cyclic patterns when LiCl and tall larkspur were used as the toxic agents. When larkspur was given as a single dose mixed with water, the lowest threshold for effects was about 14 mg/kg. We have noted significant reductions in operant responding when cattle were dosed with 14–18 mg toxic alkaloid, but no clinical signs were noted (Pfister and Cheney, 1997). Periods of reduced consumption after ingesting the larkspur toxin probably allow animals time to recover from food-specific illness and detoxify after the toxic insult.

Other studies have shown variable or cyclic food intake patterns in response to ingestion of toxic foods. Dietary diversity may result in part because herbivores limit consumption of specific toxic plants (Freeland and Janzen, 1974). Mice attempted to minimize toxic effects by varying dietary intake of toxic foods (Freeland and Saladin, 1989). Kyriazakis and Emmans (1992) reported that pigs showed a cyclic intake pattern when given rapeseed-based food. Nutritional deficiencies such as imbalances of zinc can reliably provoke cyclic food intake patterns similar to toxicoses from food (Wallwork et al., 1981).

We did not determine how cattle become adverse to tall larkspur and not other plants during peak larkspur ingestion, but two variables may be important: (1) the amount of larkspur eaten during a meal compared to the amount of other foods eaten (e.g., goats acquire an aversion to the food eaten in the greatest amount when toxicosis follows a meal of novel foods) (Provenza et al., 1994); and (2) prior illness associated with larkspur ingestion (e.g., lambs avoid the food that made them ill in the past when toxicosis follows a meal of several foods) (Burritt and Provenza, 1991, 1996). Thus, the proportion of tall larkspur eaten and prior illness associated with larkspur may cause cattle to limit intake of larkspur and not other plants.

Why do animals continue to consume a food that has been aversive in the recent past? Many toxic compounds cause food aversions (Riley and Tuck, 1985), but sampling can quickly extinguish the aversion (Provenza et al., 1992; Ralphs and Olsen, 1990). In the case of larkspur, it appears that cattle begin sampling the food because ingestion of low to moderate amounts causes few or no adverse effects while simultaneously providing energy. Increased consumption probably results in heightened adverse effects because of the dose–response nature of diterpenoid alkaloids (Manners et al., 1992, 1993). We speculate that above the 14–18 mg/kg threshold, larkspur alkaloids interact with cholinergic receptors in the gastrointestinal tract and produce nausea. However, highly nutritious larkspur also provides sufficient positive postingestive feedback for animals to quickly extinguish a food aversion and resume consumption once the gastrointestinal distress passes. Learned aversions to larkspur formed in a pen situation are quickly extinguished under field conditions when cattle begin sampling the plant (Lane et al., 1990; Ralphs and Olsen, 1990). Although the results of experiments 2 and 3 may have changed slightly had animals been given the basal food ad libitum, we believe that the basic pattern would not have changed since the degree of dietary restriction was not great. This conclusion is supported by the results from experiment 1 where animals were given food ad libitum.

duToit et al. (1991) found a similar fluctuating pattern of food ingestion in sheep given LiCl-treated feed. They noted that LiCl intake fluctuated around 39 mg/kg, a level just below a dose necessary to form a mild aversion. We found that at the highest LiCl dose, cattle averaged 37 mg/kg of LiCl per day. This suggests that mechanisms for food aversion learning are about as sensitive in cattle as in sheep or goats (duToit et al., 1991).

Why then are about 5% of animals killed by overingestion of larkspur each summer on western US mountain ranges (Ralphs et al., 1988)? The reasons why some animals fail to learn to avoid lethal doses of toxic plants are complex (Provenza et al., 1992). Our observations indicate that many cattle deaths occur during brief (i.e., 20–30 min) episodes of frenetic overingestion, when environmental circumstances apparently alter plant acceptability (Pfister et al., 1988a). At other times, cattle overingest tall larkspur for several hours when the plant is apparently very palatable, and animals that are more susceptible are sometimes fatally poisoned (Pfister, unpublished observations). Other extenuating circumstances that may play a role in cattle deaths are bloat and handling stress, but these have not been studied.

Based on the results of these trials and previous dosing experiments with tall larkspur, there appear to be at least three distinct thresholds involved in tall larkspur toxicosis (Figure 7): first, a subclinical toxicosis that results in reduced tall larkspur intake for one to three days, but no overt signs nor overall reductions in intake of safe foods (14–21 mg/kg); second, a short-acting toxicosis with overt clinical signs that results in reduced food intake for several days, but no long-term effects (near 22 mg/kg); and third, a potentially fatal toxicosis with severe clinical signs that can result in death ( ≥40 mg/kg). Obviously, there is a dose–response gradient with respect to severity of clinical signs as the dose increases above 22 mg/kg. We conclude that cyclic consumption enables cattle to generally regulate larkspur consumption below the second threshold. This

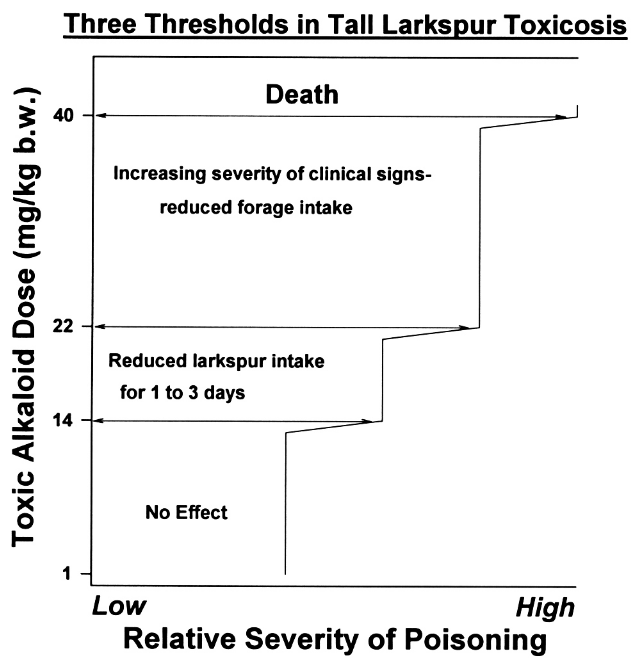


FIG. 7. Representation of three thresholds in tall larkspur toxicosis. The $y$ axis is amount of toxic alkaloid ingested, and the $x$ axis represents increasing severity of intoxication. The thresholds are: first, a subclinical toxicosis that results in reduced tall larkspur intake for one to three days, but no overt signs or overall reductions in intake of safe foods (14–21 mg/kg); second, a short-acting toxicosis with overt clinical signs that results in reduced food intake for several days, but no long-term effects (near 22 mg/kg); and third, a potentially fatal toxicosis with severe clinical signs that can result in death at ≥40 mg/kg. Severity of clinical signs increases in a dose-dependent manner above the 22 mg/kg threshold, until animals die from respiratory failure.

allows most cattle the opportunity to use an otherwise nutritious, but potentially toxic, plant. Additional research is needed to better define when this process is upset and animals are lethally poisoned.

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